



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,893	01/17/2001	Shih-Chieh Hung	11709-003001	6011
7590 08/18/2008				
Shih-Chieh Hung Dept. of Orthop. and Traumatology, Vet. General 201, Sec. 2, Shih-pai Road Hospital-Taipei Taipei, 11217 TAIWAN			EXAMINER DUNSTON, JENNIFER ANN	
			ART UNIT 1636	PAPER NUMBER
			MAIL DATE 08/18/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/761,893

Applicant(s)

HUNG ET AL.

Examiner

Jennifer Dunston, Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) ____ is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/13/2008 has been entered.

Receipt is acknowledged of an amendment, filed 3/13/2008, in which claim 1 was amended. Currently, claims 1, 4, 6, 9-20, 32 and 33 are pending.

Election/Restrictions

Applicant elected Group I without traverse in the reply filed on 9/4/2001.

Claims 12-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/4/2001.

Currently, claims 1, 4, 6, 9-11, 32 and 33 are under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6, 9, 11, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Rieser et al (US Patent No. 6,242,247 B1, cited in a prior action; see the entire reference) and Burkiitt et al (Wheater's Functional Histology (1993), page 60, cited in a prior action). This rejection was made in the Office action mailed 9/19/2007 and is reiterated below.

Caplan et al teach a method for recovering mesenchymal stem cells from human bone marrow aspirate from iliac crest, femora, tibiae, spine, rib or other medullary spaces, comprising the steps of (i) providing the bone marrow aspirate, which is a cell mixture comprising mesenchymal stem cells and other types of cells, (ii) seeding the cell mixture in a device comprising an upper plate comprising a Leukosorb™ filter, which contains pores through which other cells, such as fat cells and red blood cells, pass through, and which retains the mesenchymal stem cells, which adhere to the Leukosorb™ filter, and (iii) recovering the mesenchymal stem cells from the Leukosorb™ filter (upper plate) (e.g., column 45, line 41 to column 46, line 34). The specification does not explicitly define the term "culture device." Given the broadest reasonable interpretation of the term, the device comprising the bone marrow

aspirate or bone marrow culture of Caplan et al is a culture device. Caplan et al teach the further enrichment of mesenchymal stem cells from the cell population recovered from the Leukosorb™ filter specifically by passage over porous hydroxyapatite granules and by monoclonal antibody separation (e.g., column 46, lines 11-61). Further, Caplan et al teach that human mesenchymal stem cells isolated by their methods can be cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing 1 g/L of glucose and supplemented with 10% fetal bovine serum to allow the mesenchymal stem cells to grow without differentiation and to allow the direct adherence of only the mesenchymal stem cells to the plastic or glass surface of the culture dish (e.g., column 8, line 20 to column 9, line 45). Further, Caplan et al teach that culturing in DMEM containing 1g/L glucose makes it possible to separate mesenchymal stem cells from other cells such as red and white blood cells, other differentiated mesenchymal stem cells, etc., which are present in bone marrow (e.g., column 8, lines 20-45). Caplan et al teach the removal of the non-adherent matter (i.e., medium and cells that are not adherent) from the culture dish (e.g., column 2, lines 3-19). Thus, Caplan et al generally teach that mesenchymal stem cells can be further enriched by passage over porous hydroxyapatite granules, by monoclonal antibody separation, and by selective adherence in DMEM with glucose and fetal bovine serum. Caplan et al teach that the mesenchymal stem cells can differentiate into bone, cartilage or adipose tissue (e.g., column 1, lines 40-52; column 47, lines 9-48).

Caplan et al do not specifically teach the method where the cells that pass through the pores of the top plate collect on a lower plate base. Caplan et al do not specifically teach culturing the mesenchymal stem cells on the top plate in 10% fetal bovine serum-supplemented

Dulbecco's modified Eagle's medium containing 1 g/L glucose and do not teach removing cells not adhered on the top plate by changing a culture medium.

Rieser et al teach a method comprising the steps of (i) providing bone marrow using a method known in the art, (ii) introducing the bone marrow comprising mesenchymal stem cells to a cell space (1), closing the cell space, and introducing it into the culture medium, which results in the introduction of mesenchymal stem cells above a bone substitute plate (7) (upper plate) and a bottom plate, which is the bottom of the culture dish (e.g., column 5, lines 15-36, column 6, line 56 to column 7, line 3; Figure 1). Rieser et al teach that the cells in the cell space settle on the bone substitute plate (7) due to the effects of gravity (e.g., column 7, lines 24-34). Once the cells have settled on the plate, they adhere and grow (e.g., column 7). Rieser et al teach the subsequent removal of cartilage formed from the cells introduced into the cell space (e.g., paragraph bridging columns 6-7). Rieser et al teach that the bone substitute plate (7) serves two functions: it is a permeable wall for the cell space (1), and it provides a substrate for the adherence of cells (e.g., column 7, lines 7-24). With respect to the porosity of the upper plate (7), Rieser et al teach pores of 1 to 20 μm are suitable, as well as pores between 20 and 50 μm (e.g., column 7, lines 34-54).

Burkitt et al teach that red blood cells are 6.7-7.7 μm in diameter and nucleated cells have a diameter greater than 7.7 μm (page 60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the bone marrow aspirate into the cell space and culture dish taught by Rieser et al because Caplan et al teach it is within the ordinary skill in the art to use a filter to remove

red blood cells from bone marrow aspirate and Riser et al teach the use of a porous filter, where the pore diameter can be modified, in combination with the teachings of Burkitt et al, to allow red blood cells to pass through the pores while the nucleated cells remain on the filter. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Dulbecco's modified Eagle's medium containing 1 g/L glucose supplemented with 10% fetal bovine serum (DMEM-LG with 10% FBS), taught by Caplan et al, in the culture dish and cell space, because Rieser et al teach culturing the cells in the dish in the presence of medium. Moreover, it would have been obvious to change the medium to allow the continued growth of the cells in an undifferentiated state while removing other non-adherent, non-mesenchymal stem cells.

One would have been motivated to make such a modification in order to receive the expected benefit of eliminating the extra steps of washing the cells from the filter and performing subsequent purification steps as taught by Caplan et al. The use of the DMEM-LG with 10% FBS and media changes would result in an enriched population of cells. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Rieser et al (US Patent No. 6,242,247 B1, cited in a prior action; see the entire reference) and Burkitt et al (Wheater's Functional Histology (1993), page 60, cited in a prior action) as applied to claims 1,

4, 6, 9, 11, 32 and 33 above, and further in view of Pittenger et al (Science, Vol. 284, pages 143-147, 1999, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 9/19/2007 and is reiterated below.

The combined teachings of Caplan et al, Rieser et al, and Burkitt et al et al are described above and applied as before.

Caplan et al, Rieser et al, and Burkitt et al do not specifically teach that the mesenchymal stem cells are CD34-.

Pittenger et al teach the isolation of human mesenchymal cells from bone marrow taken from the iliac crest (e.g., page 143, right column). Pittenger et al teach that the mesenchymal stem cells are CD34- (e.g., paragraph bridging pages 143-144). The mesenchymal stem cells isolated by Pittenger et al are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically use a bone marrow aspirate from human iliac crest, because Caplan et al and Pittenger et al teach the use of bone marrow from iliac crest to isolate mesenchymal stem cells that are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute iliac crest bone marrow for any other type of bone marrow to achieve the predictable result of recovering CD34- mesenchymal stem cells that are also capable of differentiating to adipose, cartilage or bone tissue.

Claims 1, 4, 6, 9, 11 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Butz et al (US Patent No. 5,272,083; see the entire reference). This is a new rejection.

Caplan et al teach a method for recovering mesenchymal stem cells from human bone marrow aspirate from iliac crest, femora, tibiae, spine, rib or other medullary spaces, comprising the steps of (i) providing the bone marrow aspirate, which is a cell mixture comprising mesenchymal stem cells and other types of cells, (ii) seeding the cell mixture in a device comprising an upper plate comprising a Leukosorb™ filter, which contains pores through which other cells, such as fat cells and red blood cells, pass through, and which retains the mesenchymal stem cells, which adhere to the Leukosorb™ filter, and (iii) recovering the mesenchymal stem cells from the Leukosorb™ filter (upper plate) (e.g., column 45, line 41 to column 46, line 34). Caplan et al teach the further enrichment of mesenchymal stem cells from the cell population recovered from the Leukosorb™ filter specifically by passage over porous hydroxyapatite granules and by monoclonal antibody separation (e.g., column 46, lines 11-61). Further, Caplan et al teach that human mesenchymal stem cells isolated by their methods can be cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing 1 g/L of glucose and supplemented with 10% fetal bovine serum to allow the mesenchymal stem cells to grow without differentiation and to allow the direct adherence of only the mesenchymal stem cells to the plastic or glass surface of the culture dish (e.g., column 8, line 20 to column 9, line 45). Further, Caplan et al teach that culturing in DMEM containing 1g/L glucose makes it possible to separate mesenchymal stem cells from other cells such as red and white blood cells, other differentiated mesenchymal stem cells, etc., which are present in bone marrow (e.g., column 8, lines 20-45).

Caplan et al teach the removal of the non-adherent matter (i.e., medium and cells that are not adherent) from the culture dish (e.g., column 2, lines 3-19). Thus, Caplan et al generally teach that mesenchymal stem cells can be further enriched by passage over porous hydroxyapatite granules, by monoclonal antibody separation, and by selective adherence in DMEM with glucose and fetal bovine serum. Caplan et al teach that the mesenchymal stem cells can differentiate into bone, cartilage or adipose tissue (e.g., column 1, lines 40-52; column 47, lines 9-48).

Caplan et al do not specifically teach the method where the cells that pass through the pores of the top plate collect on a lower plate base. Caplan et al do not specifically teach culturing the mesenchymal stem cells on the top plate in 10% fetal bovine serum-supplemented Dulbecco's modified Eagle's medium containing 1 g/L glucose and do not teach removing cells not adhered on the top plate by changing a culture medium.

Butz et al teach a cell culture device that comprises a cell retention element detachably attached to a hanger (e.g., Abstract; Figure 2). The cell retention element includes a porous membrane growth surface (e.g., column 1, lines 56-57; column 3, lines 50-62). Butz et al teach that the tissue growth membrane may be formed of any material capable of supporting cells substantially isolated from direct contact with the medium in the well, while allowing at least a selected material to pass through and contact the cells (e.g., column 6, lines 17-22). Suitable materials include porous inert film, hydrated gels, or layered combinations such as a gel supported on a screen (e.g., column 6, lines 22-24). Butz et al teach the culture of cells on the membrane and changing the medium in the well containing the cultured cells (e.g., column 6, lines 38-61; column 11, lines 4-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the bone marrow aspirate into the retention element of the culture dish taught by Butz et al because Caplan et al teach it is within the ordinary skill in the art to use a filter to remove fat cells and red blood cells from bone marrow aspirate and Butz et al teach culturing cells in a device comprising a porous filter. It would have been obvious to one of skill in the art to use the Leukosorb filter of Caplan et al, because Butz et al teach the use of any porous inert film, and Caplan et al teach that the Leukosorb filter is suitable for the separation of human mesenchymal stem cells from fat cells and red blood cells. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Dulbecco's modified Eagle's medium containing 1 g/L glucose supplemented with 10% fetal bovine serum (DMEM-LG with 10% FBS), taught by Caplan et al, in the culture dish of Butz et al, because Butz et al teach culturing the cells in the dish in the presence of medium. Moreover, it would have been obvious to change the medium to allow the continued growth of the cells in an undifferentiated state while removing other non-adherent, non-mesenchymal stem cells, as taught by Caplan et al, because Butz et al teach it is within the skill of the art to change the medium in the culture dish.

One would have been motivated to make such a modification in order to receive the expected benefit of eliminating the extra steps of washing the cells from the filter and performing subsequent purification steps as taught by Caplan et al. The use of the DMEM-LG with 10% FBS and media changes would result in an enriched population of cells. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any

evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Butz et al (US Patent No. 5,272,083; see the entire reference) as applied to claims 1, 4, 6, 9, 11 and 32 above, and further in view of Pittenger et al (Science, Vol. 284, pages 143-147, 1999, cited in a prior action; see the entire reference). This is a new rejection.

The combined teachings of Caplan et al and Butz et al are described above and applied as before.

Caplan et al and Butz et al do not specifically teach that the mesenchymal stem cells are CD34-.

Pittenger et al teach the isolation of human mesenchymal cells from bone marrow taken from the iliac crest (e.g., page 143, right column). Pittenger et al teach that the mesenchymal stem cells are CD34- (e.g., paragraph bridging pages 143-144). The mesenchymal stem cells isolated by Pittenger et al are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically use a bone marrow aspirate from human iliac crest, because Caplan et al and Pittenger et al teach the use of bone marrow from iliac crest to isolate mesenchymal stem cells that are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to

substitute iliac crest bone marrow for any other type of bone marrow to achieve the predictable result of recovering CD34- mesenchymal stem cells that are also capable of differentiating to adipose, cartilage or bone tissue.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Butz et al (US Patent No. 5,272,083; see the entire reference) as applied to claims 1, 4, 6, 9, 11 and 32 above, and further in view of Pall (US Patent No. 4,923,620; see the entire reference). This is a new rejection.

The combined teachings of Caplan et al and Butz et al are described above and applied as before.

Caplan et al and Butz et al do not specifically teach the pore size of the Leukosorb filter.

Pall teaches filters to remove leukocytes from whole blood, where the pore diameter is from about 4 to about 8 micrometers, from about 4 to about 5.5 micrometers, or from about 6 to about 8 micrometers (e.g., column 9, lines 37-57).

Because Caplan et al and Pall teach filters to remove leukocytes, and Caplan teaches that this type of filter can be used to isolate mesenchymal stem cells, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a pore size of about 4 to about 8 micrometers in the method of Caplan et al and Butz et al to achieve the predictable result of separating mesenchymal stem cells from red blood cells and fat cells.

Response to Arguments - 35 USC § 103

With respect to the rejection of claims 1, 4, 6, 9, 11, 32 and 33 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Rieser et al (US Patent No. 6,242,247 B1), and Burkitt et al, Applicant's arguments filed 3/13/2008 have been fully considered but they are not persuasive.

The response notes that Rieser et al teach a bone substitute plate (7) with surface pores (surface roughness). The response asserts that it would be very difficult, if not impossible, to recover cells from the bone substitute plate (7) of Rieser et al. The response asserts that US Patent No. 5,634,879, US Patent No. 6,372,494, and three scientific articles to demonstrate that surface roughness assists the attachment of cells. These references do not provide evidence that mesenchymal stem cells cannot be recovered from rough cell culture surfaces. Furthermore, Caplan et al teach the removal of cells from culture dishes using a releasing agent such as trypsin with EDTA or a chelating agent such as EGTA (e.g., column 12, lines 26-41). One would expect some mesenchymal stem cells to be recovered using this method.

The response essentially asserts that one would not think to use the bone plate of Rieser et al as a filter. This is not found persuasive. It would be within the skill of the art at the time the invention was made to use a porous plate as a filter. The prior art (Muschler et al. US Patent No. 5,824,084, of record) teaches the use of a bone substitute plate as a filter that selectively retains connective tissue progenitor cells (e.g., Examples 1-2; Table 1). Accordingly, one of ordinary skill in the art at the time the invention was made would have predictably used the bone substitute plate of Rieser et al as a filter.

The response asserts that the filter of the instant invention has a greater recovering efficiency. However, the specification does not disclose the material that is used as the porous plate and does not disclose the surface roughness of the plate. Even if decreased surface roughness results in unexpected or superior results, the evidence presented must be commensurate in scope with the claims. The instant claims do not limit the surface roughness of the porous plate.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Rieser et al (US Patent No. 6,242,247 B1), Burkitt et al, and Pittenger et al, Applicant's arguments filed 3/13/2008 have been fully considered but they are not persuasive for the reasons set forth above. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Voitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1636

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636